Remarks:

Claims

By the present amendment claims 52-56 have been added. Claims 25, 27, 29, 31-32, 35, 40-41, 43 and 47-56 are pending.

Support for the recitation of recombinant polypolypeptide in the new claims can be found in, for example, ¶¶ 1, 10, 34, 37, 40, 167-169. No new matter is added.

Claim Rejections - 35 U.S.C. §112, First Paragraph - Enablement

Claims 25, 27, 29, 31, 32, 35, 40, 41, 43 and 47-51 stand rejected under 35 U.S.C. §112, first paragraph, based on an assertion that the specification, while being enabling for a polypeptide consisting of the sequence of the amino acid SEQ ID NO: 2, a fusion protein comprising the amino acid sequence SEQ ID NO:2, and an immunogenic composition comprising the amino acid sequence SEQ ID NO:2 does not reasonably provide enablement for an isolated polypeptide that comprises a fragment of at least 15 or 20 contiguous amino acids of SEQ ID NO:2, fusion protein or immunogenic composition comprising said fragments.

The rejection includes a general discussion of the unpredictability of protein chemistry, and on the consequences of a single change in an amino acid residue on the biological activity of a protein. The Office Action notes that the specification fails to disclose whether the recognizes antibodies that are obtained from individual infected with *Neisseria*. Furthermore, the Office Action asserts that the specification fails to disclose a description of fragments that are capable of binding to the antisera raised against full-length polypeptide, and thus fails to enable fragments and uses of the claimed polypeptide. Finally, the Office Action alleges that the skilled artisan would be forced into undue experimentation to practice the invention as claimed.

The Office Action notes that Applicant's argument has been considered but is not deemed persuasive. The Office Action's reply to Applicant's argument of 4/19/04 appears to have two main parts, a first part addressing a specific screening method used to evaluate peptide sequences against antisera raised against a whole peptide antigen, and a second part that concerns enablement of peptide antigens against T-cell mediated immune responses.

In the first part, the Office Action notes that Geysen et al., *Proc. Natl. Acad. Sci. USA* **1984**, *81*, 3998-4002 discloses scanning specific peptide sequences against antisera to the whole antigen. Further, the peptide sequences screened in Geysen et al. are said to consist only of the

peptide and nothing else of the antigen, while Applicant's claimed invention, it is asserted, comprises fragments of 15 or 20 contiguous amino acids of SEQ ID NO:2, but also other unknown amino acids, and thus can bind to any antibody in a non-specific manner.

If the Office Action's contention is that the claims are not enabled for mixtures of fragments of SEQ ID NO:2, Applicant respectfully disagrees. The claimed invention includes immunogenic fragments of SEQ ID NO:2 (when administered to a subject in a suitable composition which can include an adjuvant, or a suitable carrier coupled to the polypeptide) induces an antibody or T-cell mediated immune response that recognizes the polypeptide SEQ ID NO:2. Consequently, the claimed polypeptide requires induction of a specific immune response and not merely that it bind non-specifically to any antibody.

In the second part of the reply to Applicant's argument of 4/19/04, the Office Action asserts that the specification fails to provide adequate guidance to enable the use of the claimed polypeptide in stimulating and/or expanding T-cells specific for a *Neisseria* antigen. The Office Action cites the difficulty in inducing and expanding T-cells to peptide epitopes because of the requirements for protein processing, handling by antigen presenting cells, peptide interaction with major histocompatibility proteins and recognition by T-cells. The Office Action asserts that interaction of T-cells and antigen presenting cells with bacterial proteins is complex.

Applicants note that the art has recognized the difficulties associated with processing of protein fragments, and has devised methods for overcoming inefficient processing of protein fragments in studies of human T-cell responsiveness. These methods were available at the time of the filing of the instant application and were within the purview of those of skill in the art. For instance, in Reece et al., *J. of Immunol.* **1993**, 6175-6184 (which was attached as Exhibit A in Applicant's amendment of 4/19/04) the difficulties associated with inefficient protein processing in connection with studies of T-cell responsiveness were recognized (p. 6175, ¶ 1). In Reece et al., the difficulties of protein processing were overcome by synthesizing overlapping dodecapeptides on pins to map T-cell epitopes of tetanus toxin. Pools of 20 peptides each were used to simplify the mapping assays. Thus, it was practical to synthesize a large number of peptides, and the initial screen needed only to assay sixty to seventy pools. Pools that generated strong responses were deconvoluted by assaying the members of the pool. That such experimentation using a multipin method to screen for antigens is ordinary in this art is

illustrated in *Current Protocols in Immunology* **1997** 9.7.1-9.7.19 (which was attached as Exhibit B to the amendment of 4/19/04) and Reece et al., 172 *J. of Immunol.* **1994** 241 (previously attached as Exhibit C). Consequently, given the teachings of the specification that includes the structural formula of SEQ ID NO:2 and experimental methods well-known in the art at the time of filing, Applicants assert that the claimed polypeptides are enabled.

In light of the above discussion, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph is respectfully requested.

FEE DEFICIENCY

☒ If an extension of time is deemed required for consideration of this paper, please consider this paper to comprise a petition for such an extension of time; The Commissioner is hereby authorized to charge the fee for any such extension to Deposit Account No. 50-0258.

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Closing Remarks

Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration in view of this response and allowance of the pending claims are earnestly solicited.

Respectfully submitted,

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